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Full Length Research Paper

Prevalence and risk factors of anaemia among human immunodeficiency virus (HIV)-infected antiretroviral therapy naïve children in Makurdi, Nigeria: A retrospective study

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Anaemia is a common condition in human immunodeficiency virus (HIV) infection and it contributes significantly to its morbidity and mortality. However, there are a few available studies describing the risk factors of anaemia in HIV- infected, antiretroviral therapy naïve (ART) Nigerian children. A retrospective, cross-sectional study, at the Federal Medical Centre, Makurdi, between June, 2010 and June, 2012.Potential risk factors of anaemia were tested for significance in bivariate and multivariate logistic regression analyses. 403 HIV-infected children, including 210 males and 193 females, aged between 4 months to 15 years were studied. The child's age and gender, growth failure, CD4 counts, viral load, tuberculosis and other co-morbidities, family HIV status and other socioeconomic factors were not significantly associated with anaemia. The high prevalence of anaemia in this study supports the routine pre-ART evaluation for anaemia, so that the preferred first line antiretroviral medicines would be those not associated with anaemia. Also, in this setting, concerted efforts should be put in place to specifically screen for anaemia among at risk HIV-infected children living in urban communities and/or those co-infected with hepatitis B infection. Programmatic interventions including preventive haematinics and micronutrients supplements will be better guided to at risk children.

Key words: Human immunodeficiency virus (HIV)-infection, anti-retroviral naïve, children, anaemia, risk factors, Makurdi, Nigeria.

INTRODUCTION

Among the 20 Global Plan Priority Countries (GPPC), Nigeria had shown a slow decline of 8% of new human immunodeficiency virus (HIV) infection among children between 2009 and 2012 (UNAIDS, 2013). Also with the poor access and uptake of prevention of mother to child transmission of HIV interventions in Nigeria, the global target of a decline of 50% of new paediatric HIV infection in GPPC, sets for between 2009 and 2015, is unlikely to be reached (National Agency for the Control of AIDS, 2012; UNAIDS, 2013). Regional differences in the HIV burden also exist in Nigeria (Federal Ministry of Health, 2010a). According to the National Sentinel Survey among

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pregnant women in antenatal care in Nigeria, Benue State, located in the North Central region, has the highest HIV prevalence rates of 10% in 2005, 10.6% in 2008 and 12.7% in 2010 (Federal Ministry of Health, 2010a). The high level of poverty and illiteracy, some socio-cultural practices and the lack of financial empowerment in women are some of the reasons adduced for the high prevalence of HIV in Benue State (Ojoawo et al., 2005).

Anaemia is a common condition in HIV infected children (Totin et al., 2002; Eley et al, 2002; Adewuyi and Chitsike, 1994; Ellaurie et al., 1990; Adetifa et al., 2006; Okechukwu et al., 2010; Shet et al., 2009). Anaemia also contributes significantly to the morbidity and mortality in HIV-infection (Duong et al., 2008). In addition, regardless of its aetiology, anaemia in children has been related to reduced work performance, reduced cognitive functions, growth retardation, and impaired immune systems (Calis et al., 2008).

The pathogenesis of anaemia in HIV-infection includes a combination of nutrient deficiencies, HIV-mediated suppression of erythropoiesis, drug effects (cotrimoxazole), other opportunistic infections and HIV-associated malignancies (Okechukwu et al., 2010; Idro, 2003). In resource-limited settings including Nigeria, the prevalence is even higher because of pervasive micronutrient deficiencies (iron, folic acid, zinc and vitamin A deficiencies), malaria, sickle cell anaemia and helminthiasis (Okechukwu et al., 2010).

Available data in Nigeria revealed that the burden of anaemia in children with HIV is high; at between 52.5 and 77.9%, depending on the definitions ascribed to anaemia (Adetifa et al., 2006; Okechukwu et al., 2010; Ezeonwu et al., 2014). Likewise, the rate of anaemia was also high at 76.1% among the preschool Nigerian children in the general population (WH0, 2008).

This study seeks to document for the first time, the prevalence and risk factors of anaemia among HIV-infected antiretroviral therapy naïve children in Makurdi, the capital of Benue State (one of the 12+1 States, which had consistently contributed immensely to the high burden of HIV in Nigeria (UNAIDS, 2013); thereby adding to the pool of available data in Nigeria.

The need for the study is also strengthened by the fact that the socio-economic factors that impact on the burden of anaemia (Saloojee et al., 2007; Normén et al., 2005; Mpontshane et al., 2008) also vary from one setting to another, even in the same country.

MATERIALS AND METHODS

Study design

It was a retrospective cross-sectional study among HIV-infected antiretroviral (ART) naive children.

Study area

The study took place between June 2010 and June 2012 at the Paediatric ART Clinic of the Federal Medical Centre (FMC), Makurdi; the capital city of Benue State. It provides tertiary level of paediatric HIV services to the people residing in Makurdi and the surrounding rural communities. The facility is supported by the AIDS Prevention Initiative in Nigeria (APIN)/Harvard PEPFAR (The USA President's Emergency Plan for AIDS Relief) programme. Benue State lies within the middle belt region of Nigeria. Its geographic coordinates are longitude 7° 47' and 10° 0' East, latitude 6° 25' and 8° 8' North. The state has a population of over 5 million and occupies a landmass of 34,059 km^2. The state experiences two distinct seasons, the wet/rainy season and the dry/summer season. The rainy season lasts from April to October with annual rainfall in the range of 100 to 200 mm. The dry season begins in November and ends in March. Temperatures fluctuate between 23 and 37°C.

Participants

Included in the study were HIV infected children (≤15 years of age) who were antiretroviral naïve and whose: haemoglobin (Hb) concentration values; physical growth parameters; socio-demographic factors; and records of other potential risk factors (that is, co-morbidities/opportunistic infections) of anaemia, were available on enrollment into our ART programme. HIV-infected antiretroviral naïve children with no Hb value and incomplete records of potential risk factors were excluded. Also excluded were HIV-infected treatment experienced children.

Recruitment of subjects and data collection

FMC, Makurdi provides paediatric HIV care and treatment in accordance with the Nigerian Guidelines on Paediatric HIV/AIDS Treatment and Care (Federal Ministry of Health, 2007, 2010b). Children were recruited into care and treatment if they were confirmed to be HIV infected. All subjects ≥18 months had an initial double rapid HIV antibody test using Determine™ HIV 1/2 first and then HIV 1/2STAT-PAK™. HIV infection was confirmed in those with a reactive rapid test by the Western Blot test. Two HIV DNA PCR positivity tests for those <18 months confirmed HIV infection in this age group. A study proforma was developed to capture the following information that had been recorded on the subjects' Initial Clinical Evaluation Form (ICEF) at enrollment into our programme: mode of HIV transmission; caregivers' HIV status; whether caregiver is on ART or not; marital status of the caregivers; place of residence (rural versus urban); number of people in the household; orphanhood status of the child; demographic factors of the child; mode of infant feeding among the under-fives; World Health Organization (WHO) HIV/AIDS paediatric stage; anthropometric measurements; and other diagnosed co-morbidities/opportunistic infections. These co-morbidities/opportunistic infections include tuberculosis, oro-pharyngeal and oesophageal candidiasis, diarrheal disease, presumed sepsis, malaria fever, pneumonia, hepatitis B surface antigen and hepatitis C virus antibodies.

Operational definitions

For the purpose of the study, the following terms were defined: HIV infected ART-naive children were HIV infected children who had received no prior antiretroviral drugs, except for prevention of mother-to-child transmission (PMTCT)

A maternal orphan is the child whose mother has died. A paternal orphan is the child whose father has died. A double orphan is the child whose both father and mother have died. Caregiver (CG) is a person who has consistently assumed responsibility for the housing, health, or safety of the child (individuals who administered the child medication daily and bringing the child for clinic appointments).

This may be the parents of the child or a biological or a non-biological relation if the child happens to be an orphan. Exclusive breastfeeding (EBF) was defined as the infant receiving only breast milk from his/her mother and no other liquids or solids, with the exception of drops or syrups consisting of vitamins, mineral supplements, or drugs (Gaillard et al., 2001).

Exclusive breast milk substitute feeding (EBMS) was defined as provision of infant formula and the exclusion of all breastfeeding (Gaillard et al., 2001). Mixed feeding (MF) was defined as giving breast milk with breast milk substitute or other liquids or solid foods (Gaillard et al., 2001). Two episodes of instances of mixed feeding were required for this definition.

Anaemia in children was as previously defined by Adetifa et al. (2006) and Kiggundu et al. (2013). It includes anaemia when the haemoglobin concentration was less than 10 g/dl; mild anaemia when the haemoglobin value was between 8 and 9.9 g/dl; moderate anaemia with haemoglobin values between 6 and 7.9 g/dl and severe anaemia when haemoglobin is <6 g/dl.

To define under-nutrition in children less than 5 years, anthropometric computations and comparisons were conducted for the weight for age z-score (WAZ-score) and height for age z-score (HAZ-score) using the WHO Anthro software which is based on WHO child growth standards of 2006 (World Health Organization, 2011). Underweight was defined as a weight for age z-score (WAZ-score) less than -2 standard deviations (SD) from the WHO reference median values. Stunting was defined as height for age z-score (HAZ-score) less than -2 SD from the reference values. Weight for height z-score (WHZ-score) less than -2 SD from the WHO reference median defined wasting.

For children ≥5 years, the body mass index (BMI) was calculated as the weight in kilograms divided by the square of the height in meters (kg/m^2). Values <18.5 defined undernutrition, values >25 was overweight and values >30 was obesity (World Health Organization, 1995). Diarrhea was defined as the passage of three or more loose or watery stools during a 24-h period. Chronic diarrhoea defined as persistent diarrhoea 14 days or more. Definition of clinical sepsis at enrollment was limited to the presence of two or more of the following: abnormal temperature (< 36.0°C or >38.3°C) or age specific tachycardia (>140 beat/min for 0 to 2 years, >120 for 2 to 6 years and >110 for >6 years) or acute altered mental status; with a clinical suspicion of new infection including cough/chest pain and or abdominal pain/distension/diarrhoea and/or dysuria and or headache with neck stiffness and/or presence of cellulitis/wound infection/joint infection (Daniels , 2011).

Acute respiratory infection (pneumonia) was made if the child present with cough (less than 72 hours), fever, tachypnea, and focal pulmonary findings on physical examination. Presumptive tuberculosis (TB) diagnosis was based on radiographic evidence indicative of TB in a child presenting with a persistent cough for more than 2 weeks and/or fever for more than 1 week and/or recent failure to thrive, together with or without a documented TB contact.

Oro-pharyngeal candidiasis is the presence of candidiasis on the tongue, buccal mucosa and the pharynx. Esophageal candidiasis is the presence of extensive oro-pharyngeal candidiasis extending down to the esophagus with accompanying difficulty in swallowing and/or painful swallowing.

Laboratory measurements

The haemoglobin concentration of the subjects was determined as part of a full blood count using the Mindray Haematology analyzer. In addition to determining the CD4 count and the viral load, venous blood samples were also collected for: malaria parasites (Giemsa stain); hepatitis B surface antigen and hepatitis C virus antibody (using the third generation ELISA technique, EIAgen HBsAg Kit, EIAgen HCV Ab Kit). All tests were done at the APIN/PEPFAR laboratory of FMC, Makurdi.

Ethical consideration

Upon recruitments into the care and ART programme, parents or caregivers of the HIV-infected children that populated the study had initially provided written informed consent (and assent from the children if ≥7 years of age) for the use of their data for research as approved by the Hospital Research and Ethics Committee of the FMC, Makurdi and the AIDS Prevention Initiative in Nigeria (APIN)/Harvard PEPFAR (The USA President's Emergency Plan for AIDS Relief) program. For this study, permission was sought for and gotten for the use of the relevant data.

Statistical analysis

Descriptive statistics were tabulated as medians for continuous variables and numbers and percentages for categorical variables. The medians were compared using the Mann-Whitney U test respectively. The main outcome variables in the analysis were anaemia versus no anaemia. The prevalence of anaemia and its severity were also calculated. Potential risk factors of anaemia were tested for significance in a bivariate logistic regression. Some of these predictive risk factors included *a priori* factors that had been found to be associated with anaemia (that is, age, gender, anemia, HBsAg, hepatitis C virus (HCV), undernutrition, WHO clinical staging, CD4 count, viral load, malaria fever, mode of infant nutrition, mode of HIV transmission, socioeconomic factors) in previous studies (Okechukwu, 2010; Shet et al., 2009; Saloojee et al., 2007; Normén et al., 2005; Mpontshane et al., 2008; Rose et al., 2014). Variables that achieved a significant level of 0.1 were considered eligible for multivariate logistic regression analysis. For all analyses, p-values less than 0.05 were considered statistically significant. Statistical analysis was done using SPSS version 16.

RESULTS

A total of 419 HIV infected children were seen within the study period but only 403 satisfied the inclusion criteria. Excluded were 10 children with incomplete data and another 6 children whose haemoglobin values were missing. The basic characteristics of these 16 children were also similar to the included subjects. Table 1 reveals that the 403 subjects were between 4 months and 15 years of age with a median age of 5 years and Interquartile range of 3 to 8. There were 210 males (M) and 193 females (F) with a M:F ratio of 1:0.9. Only 85 (21.1%) children were presented in WHO clinical stages 3 and 4. The median log10 viral load and CD4 counts were 4.73 copies/ml and 490 cell/mm^3, respectively. The prevalence of anaemia was 59.5% (that is, 240/403), including those with mild degree of anaemia, 44.5% (179/403) and those with moderate anaemia, 14.1% (57/403). Severe anaemia was only seen in 4 subjects (0.9%).

Tables 2 to 4 show the risk factors of anaemia among the subjects. These risk factors (Socio-economic and demographic, clinical/laboratory, co-morbidities/ opportunistic infections) were tested together in bivariate and multivariate analyses, but were presented in three tables for the purpose of clarity and easy understanding. In bivariate analyses, the mode of HIV transmission, the HIV status of the caregivers, the number of people living in the household, the place of residence of the child,

Table 1. Baseline characteristics of the subjects.

Characteristic	N [N/403(%)]
Range	4 months to 15 years
Median in years (IQR)	5 (3-8)
<5 years	184 (45.7)
≥5 years	219 (54.3)
Gender	
Male	210 (52.1)
Female	193 (47.9)
WHO clinical staging	
1&2	318 (78.9)
3&4	85 (21.1)
CD4 counts (cells/mm^3)	
Median (IQR)	490.0 (260.0 – 870.0)
≤200	75 (18.6)
>200	328 (81.4)
HIV viral load (copies/ml)	
Median Log10(IQR)	4.73 (3.74-5.36)
>10,000	280 (69.5)
<10,000	123 (30.5)
Haemoglobin (g/dl)	
No anaemia(≥ 10)	163 (40.5)
Anaemia (<10)	240 (59.5)
Mild anaemia (8-9.9)	179 (44.5)
Moderate (6-7.9)	57 (14.1)
Severe (<6)	4 (0.9)

IQR: Interquartile range.

the child, co-infection with Hepatitis B virus in the child, presence of oropharyngeal candidiasis in the child and presence of pneumonia in the child were found to be associated with anaemia. However, at multivariate analyses, only the number of people living in the household, the place of residence of the child and co-infection with hepatitis B virus in the child remained independently associated with anaemia. The trend was such when the number of people living in the HIV-positive household were less than 5, this tends to significantly protect against anaemia (AOR, 0.605, 95% CI; 0.390 to 0.939; P=0.025). Conversely, the likelihood of having anaemia was 1.653-fold, when the child was living in the urban community compared to a rural community (AOR; 1.653, 95% CI: 1.036-2.638; P=0.035). Furthermore, the presence of co-infection with hepatitis B virus increases the risk of anaemia by 2.318-fold. (AOR, 2.318, 95% CI: 1.173-4.580; P=0.016). The child's age and gender, CD4 counts, growth failure, tuberculosis, and other co-morbidities, family HIV status and other socioeconomic factors were not significantly associated with anaemia. Although the viral load and the CD4 count were not significantly associated with anaemia, majority of the subjects with anaemia were those with viral load >10,000 copies/ml (that is, 171 [71.35%]) and those with CD4 count ≤200 cell/mm^3 (189 [78.70%]).

DISCUSSION

In the present study, the prevalence of anaemia was 59.5% among the subjects. When compared with other studies in similarly resource constrained settings, our finding was higher than the reported prevalence of 3% by Ezeonwu et al. (2014) and the 44% by Makubi et al. (2012), but was lower than the respective values of 66, 70%, 74.6 and 77.9% reported by Shet et al. (2009), Shah and Katira (2011), Okechukwu et al. (2010) and Adetifa et al. (2006). While the higher cut off definition of anaemia (that is, less than 11 g/dl) may explain the higher prevalence of anaemia in Shah and Katira (2011) and Shet et al. (2009) studies; the burden of anaemia in our setting is definitely lower than that obtained by Adetifa et al. (2006) and Okechukwu et al. (2010) that used similar definition of anaemia of <10 g/dl. The lower prevalence reported by Ezeonwu et al (2014) is also noteworthy as a lower definition of anaemia (that is, <8 g/dl) was used, although their study included only 67 HIV-infected children. It is obvious that the different definitions ascribed to anaemia and the differing clinical and socio-economic risk factors of anaemia obtainable in different settings are responsible for the varying burden of HIV associated anaemia.

The pathogenesis of anaemia in HIV-infection had been previously summarized by Okechukwu et al. (2010) and Idro (2003). However, the advancement of the HIV disease, the presence of undernutrition, the presence of co-infections (except Hepatitis B co-infection) and other co-morbidities were not found to be independently associated with anaemia in this study. These findings are in contrast with other studies whereby the presence of tuberculosis (Swaminathan et al., 2008; Shet et al., 2009; Makubi et al., 2012), the presence of undernutrion (Shet et al., 2009) and the presence of advanced HIV disease (Ezeonwu et al., 2014; Eley et al., 2002; Adewuyi and Chitsike, 1994; Adetifa et al., 2006) were found to be significantly associated with anaemia.

Although, anaemia was found more in subjects with advanced HIV disease (that is, those with CD4 count ≤200 cell/mm^3 and viral load >10,000 copies/ml) in this study, this association was not found to be statistically significant. Totin et al. (2002) had reported a similar findings. Nevertheless, HIV infected subjects with advanced HIV disease are expected to be more at risk of anaemia because the suppression of erythro-poiesis by cytokines produced by HIV-infected lymphocytes, monocytes, and macrophages is more profound with increase in viral load and the increased number of HIV-infected

Table 2. Socio-economic and demographic risk factors of anaemia among the subjects.

Clinical variable	Anaemia (<10 g/dl)	No anaemia (≥10 g/dl)	Bivariate analysis			Multivariate analysis		
			OR	95% CI	P -value	AOR	95%CI	P-value
Demography								
Age (Years)								
Median(IQR)	5.00(3-8)	5.00(3-9)	-	(0.741 - 1.650)				
<5	112(46.7)	72(44.2)	1.10		0.142			
≥ 5 (Ref)	128(53.3)	91(55.8)	6		0.622			
Gender								
Male	128 (53.3)	82 (50.3)	1.12	(0.758 - 1.681)	0.551	-		-
Female (Ref)	112 (46.7)	81 (49.7)	9					
Family/Socio-economic factors								
Orphanhood status								
Yes	27 (11.3)	23 (14.1)	0.77	(0.425 - 1.400)	0.393	-	-	-
No (Ref)	213 (88.8)	140 (85.9)	2					
Mode of HIV transmission								
Vertical	234 (97.5)	149 (91.4)	3.66	(1.378 - 9.746)	0.006	7.88	-	0.999
Blood transfusion (Ref)	6 (2.5)	14 (8.6)	4					
Mode of infant feeding								
EBMS	175 (72.9)	124 (76.1)		-	0.169	-	-	-
MF	47 (19.6)	34 (20.9)	-					
EBF (Ref)	18 (7.5)	5 (3.1)						
Caregivers' HIV Status								
Infected	236 (98.3)	149 (91.4)	5.54	(1.791 - 17.161)	0.001	0.000	-	0.999
Not infected (Ref)	4 (1.7)	14 (8.6)	4					
Caregiver on HAART								
No	55 (23.3)	29 (19.5)	1.25	(0.758 - 2.085)	0.374	-	-	-
Yes (Ref)	181 (76.7)	120 (80.5)	7					
Marital status of caregiver								
Without partner	13 (5.4)	12 (7.4)	0.72	(0.320 - 1.622)	0.427	-	-	-
With a partner (Ref)	227 (94.6)	151 (92.6)	1					

Table 2 cont'd

No of people in the household								
>5	160 (66.7)	81 (49.7)	2.02	(1.347 - 3.044)	0.001	0.605	(0.390 - 0.939)	0.025
≤5 (Ref)	80 (33.3)	82 (50.3)	5					
Place of residence								
Urban	57 (23.8)	54 (33.1)	0.62	(0.404 - 0.978)	0.039	1.653	(1.036 - 2.638)	0.035
Rural (Ref)	183 (76.3)	109 (66.9)	9					

NA: Not applicable; IQR: interquartile range.

Table 3. Clinical/Laboratory risk factors of anaemia among the subjects.

Clinical/Laboratory variable	Anaemia (<10 g/dl)	No anaemia (≥ 10 g/dl)	Bivariate analysis			Multivariate analysis		
			OR	95% CI	P -value	AOR	95% CI	P-value
WHO Clinical staging								
3&4	55 (22.9)	30 (18.4)	1.318	(0.801 - 2.168)	0.276	-	-	-
1&2 (Ref)	185 (77.1)	133 (81.6)						
CD4 count					-			
Median(IOR)	447.0 (240.3 - 825.5)	560.0 (278.0 - 921.0)	1.563	(0.918 - 2.661)	-	0.694	0.395 - 1.218)	0.203
≤200	189 (78.7)	139 (85.3)			0.055			
>200 (Ref)	51 (21.3)	24 (14.7)			0.099			
Viral load (copies/ml)					-			
Median Log10(IQR)	4.79 (3.81 - 5.39)	4.58 (3.68 - 5.26)	1.228	(0.799 - 1.887)	-	-	-	-
>10,000	171 (71.3)	109 (66.9)			0.209			
<10,000(Ref)	69 (28.8)	54 (33.1)			0.349			
Hepatitis B surface antigen								
Yes	20 (8.3)	26 (16.0)	0.479	(0.257 - 0.891)	0.018	2.318	(1.173 - 4.580)	0.016
No (Ref)	220 (91.7)	137 (84.0)						
Hepatitis C antibodies								
Yes	7 (2.9)	2 (1.2)	2.403	(0.493 - 11.719)	0.439	-	-	-
No (Ref)	233 (97.1)	160 (98.8)						

NA: Not applicable; IQR: Interquartile range.

Table 4. Co-morbidities/Opportunistic infections and anaemia among the subjects.

Diagnosed co-morbidities/opportunistic infections	Anaemia (<10 g/dl)	No anaemia (≥ 10 g/dl)	Bivariate analysis			Multivariate analysis		
			OR	95% CI	P -value	AOR	95%CI	P-value
Tuberculosis								
Yes	46 (19.2)	22 (13.5)	1.520	(0.875 – 2.640)	0.136	-	-	-
No (Ref)	194 (80.8)	141 (86.5)						
Oropharyngeal candidiasis								
Yes	33 (13.8)	12 (7.4)	2.006	(1.003 – 4.012)	0.046	0.505	(0.241 – 1.060)	0.071
No (Ref)	207 (86.3)	151 (92.6)						
Esophageal candidiasis								
Yes	5 (2.1)	2 (1.2)	1.713	(0.328 – 8.937)	0.797	-	-	-
No (Ref)	235 (97.9)	161 (98.8)						
Diarrhoeal disease								
Yes	4 (1.7)	8 (4.9)	0.328	(0.097 – 1.109)	0.060	3.246	(0.924 – 11.401)	0.066
No (Ref)	236 (98.3)	155 (95.1)						
Sepsis								
Yes	8 (3.3)	3 (1.8)	1.839	(0.481 – 7.038)	0.554	-	-	-
No (Ref)	232 (96.7)	160 (98.2)						
Malaria fever								
Yes	31 (12.9)	22 (13.5)	0.951	(0.529 – 1.709)	0.866	-	-	-
No (Ref)	209 (87.1)	141 (86.5)						
Sickle cell disease								
Yes	3 (1.3)	6 (3.7)	0.331	(0.082 – 1.344)	0.201	-	-	-
No (Ref)	237 (98.8)	157 (96.3)						
Pneumonia								
Yes	20 (8.3)	3 (1.8)	4.848	(1.417 – 16.595)	0.006	0.158	(0.043 – 584)	0.006
No (Ref)	220 (91.7)	160 (98.2)						
WAZ								
Median(IQR)	-1.40 (-3.11 to -0.05)	-1.45 (-2.32 to -0.28)	1.435	(0.758 – 2.720)		-	-	-
<-2 SD	40 (36.7)	21 (28.8)			0.394	-	-	-

Table 4 Cont'd

≥-2 SD (Ref)	69 (63.3)	52 (71.2)			0.267
NA	-	-			
HAZ					
Median(IQR)	-2.27 (-3.98 to -0.97)	-2.11 (-4.02 to 0.30)			
<-2 SD	62 (56.9)	37 (50.7)	1.283	(0.708 – 2.327)	0.524
≥-2 SD (Ref)	47 (43.1)	36 (49.3)			0.411
NA	-	-			
WHZ					
Median(IQR)	-0.29 (-1.33 to 0.97)	0.24 (-1.05 to 1.27)			
<-2 SD	15 (13.8)	7 (9.6)	1.505	(0.581 – 3.893)	0.190
≥-2 SD (Ref)	94 (86.2)	66 (90.4)			0.397
NA	-	-			
BMI					
Median (IQR)	16.40 (14.80 -17.60)	16.20 (14.78-17.53)			
<18.5	113 (86.3)	73 (81.1)	1.462	(0.708 – 3.019)	0.973
≥18.5 (Ref)	18 (13.7)	17 (18.9)			0.303
NA	-	-			

NA: Not applicable; WHZ: weight for height Z score; SD: standard deviation; IQR: interquartile range; HAZ: height for age Z score; WAZ: weight for age Z score; BMI: body mass index.

lymphocytes, monocytes, and macrophages seen in advanced HIV disease (Ezeonwu et al., 2014; Evans and Scadden, 2000).

Furthermore, Ezeonwu et al. (2014) and Shah and Katira (2011) did not also demonstrate the association between nutritional status and Hb level in their studies. Ezeonwu et al. (2014), had earlier suggested that anthropometric assessment of nutritional status measured macronutrient deficiency, whereas anaemia result more from the deficiencies of micronutrients such as iron, vitamin B complex, and folic acid deficiencies and may thus explain this discordance.

Curiously, the presence of co-infection with hepatitis B virus increases the risk of anaemia by 2.318-fold. Whilst this association may be difficult to explain, a possibility of warm auto-immune hae-molytic anaemia (WAIHA) that has been reported in viral hepatitis B infection cannot be ruled out (Khawaja et al., 2011; Yoshioka and Miyata; 1980). WAIHA results from production of an IgG isotype autoantibody directed against unclassified red cell antigens or red cell membrane proteins and may thus explain the anaemia seen (Khawaja et al., 2011; Yoshioka and Miyata; 1980).

Furthermore, the likelihood of having anaemia was 1.653-fold when the child was living in the urban community compared to rural community. This finding is in contrasts with that of Shet et al. (2009) in India whereby there was an increased vulnerability of HIV-infected children hailing from a rural setting to developing anemia. Shet et al. (2009) attributed this rural dominance to diminished quality of nutritional intake among the rural folks; ironically, the same condition may be applicable in our own urban setting since the deterioration of the Nigerian economy of the 1980s. The caregivers of our subjects living in the rural communities are majorly farmers and their ready access to and consumption of fresh green leafy vegetables may partly explain the protection against

anaemia. Fresh green leafy vegetables have been well documented to prevent or treat anaemia among Nigerians (Oyedeji, 2005).

Furthermore, the study also showed that when the numbers of people living in the HIV-positive household were less than 5, this tends to significantly protect against having anaemia. Not surprisingly, the more mouths are to be fed, the harsher the strain on the family economy and thus the higher propensity to developing nutritional anaemia. Food security is defined as regular physical, social and economic access to sufficient quantities of safe and nutritious food, which meets the dietary requirements for a healthy life. Overpopulation in the household threatens food security and can lead to nutritional anaemia. Overpopulation also impacts negatively on family earnings; it reduces savings and assets, and reduces the money in the pocket that can be used to assess treatment for illnesses that are known to have the potential of causing anaemia (Rose et al., 2012).

Conclusion

The high prevalence of anaemia in this study supports the routine pre-ART evaluation for anaemia, so that the preferred first line antiretroviral medicines would be those not associated with anaemia. Also, in our setting, concerted efforts should be put in place to specifically screen for anaemia among HIV-infected children living in urban communities and/or those co-infected with hepatitis B infection. Programmatic interventions should also be guided by the information from this study, so that preventive haematinics and micronutrients supplements are properly directed to at risk children.

LIMITATION OF THE STUDY

Being a retrospective study, the impacts of other common determinants of anaemia in our setting, like hookworm and ascaris infestations and micronutrient (iron, vitamin B complex, and folic acid) deficiencies were not studied because stool microscopy and assessment of these micronutrients were not routinely determined on enrollment into our care and treatment programme. Likewise, morphologic characterization of anaemia was also not routinely done on enrollment into our programme, even though this would have provided a clue about the possible aetiology of the anaemia in this study.

Also, although other co-morbidities like malaria, diarrhoeal disease, sepsis were not significantly associated with anaemia on multivariate analyses, this finding should be interpreted with caution as these illnesses may have been present but had resolved in many more subjects prior to presentation at our HIV care and ART programme.

Furthermore, the lack of data on anaemia in a comparable group of HIV negative children in the same setting limits its interpretation.

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Conflict of Interest

The authors have not declared any conflict of interests

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